SHORT REPORT

Does a carpal tunnel syndrome predict an underlying disease?

Maarten C de Rijk, Frederique H Vermeij, Maartje Suntjens, Pieter A van Doorn

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Carpal tunnel syndrome (CTS) may be the presenting symptom of an underlying disease such as diabetes mellitus, hypothyroidism or connective tissue disease (CTD). It was investigated whether additional blood tests (glucose level, thyroid-stimulating hormone level and erythrocyte sedimentation rate) are useful to detect diabetes mellitus, hypothyroidism or CTD in patients with CTS who have not been diagnosed with these diseases before. A group of 516 consecutive patients electromyographically diagnosed with CTS without known diabetes mellitus, hypothyroidism or CTD underwent blood tests and were followed up for incident diabetes mellitus, hypothyroidism or CTD to investigate whether these additional blood tests are useful to detect these diseases in patients with CTS. In our CTS population, only two patients were newly diagnosed with diabetes mellitus, two with hypothyroidism and none with CTD. In general, systematic screening for incident diabetes mellitus, hypothyroidism and CTD through additional blood tests seems to be of little additional value in otherwise typical cases of CTS.

Carpal tunnel syndrome (CTS) has been reported to be associated with underlying metabolic and inflammatory conditions such as diabetes mellitus , hypothyroidism and connective tissue disease (CTD), including rheumatic disorders.[1 2] Because these diseases are common in the general population,[3–6] the question was raised as to whether CTS may be the presenting symptom in a patient with previously unknown diabetes mellitus, hypothyroidism or CTD. Thus far, no studies have been conducted dealing with this issue in a general population.[2] Therefore, we investigated whether additional blood tests (glucose level, thyroid-stimulating hormone (TSH) level and erythrocyte sedimentation rate (ESR)) could be of diagnostic value in patients with CTS who are not known to have any of these underlying diseases.

PATIENTS AND METHODS

We retrospectively evaluated a large group of consecutive patients with CTS from the Erasmus University Medical Center (Erasmus MC, Rotterdam, the Netherlands) and the Sint Franciscus Gasthuis (SFG) Hospital (Rotterdam, the Netherlands). The patients with CTS from Erasmus MC were diagnosed between 1990 and 2000 and those from the SFG Hospital between 1998 and 2001. Data were obtained from medical records. For all patients with a clinical diagnosis of CTS, whether they fulfilled the inclusion criteria for this study: clinical diagnosis of CTS confirmed by electrodiagnostic study,[7 8] and one or more of the following blood tests: (non-fasting) glucose level, TSH level or ESR. The following diseases were considered as CTD: rheumatoid arthritis, systemic lupus erythematosus, scleroderma, Sjögren's disease, gout and mixed CTD. The study population comprised both patients with a one-sided CTS as well as those with double-sided CTS. Patients with CTS and concurrent (sub) clinical polyneuropathy were not excluded from the study.

In the Erasmus MC, reference values for TSH were 0.2–4.2 mU/l; for glucose 3.5–5.6 mmol/l; and for ESR <10 mm/h in men and <20 mm/h in women. In the SFG Hospital, these values were 0.16–4.6 mU/l, 4–6.4 mmol/l, and <15 mm/h in men and <20 mm/h in women, respectively.

We defined de novo patients as those with CTS who were newly diagnosed with diabetes mellitus, hypothyroidism or CTD after the additional blood tests. To identify de novo patients in the present study, we selected all patients with CTS who had an abnormal value in at least one of the blood tests and without a previously diagnosed related underlying disorder. To come to a final diagnosis of putative underlying disease, these patients were retrospectively followed up for diabetes mellitus, hypothyroidism and CTD by checking the electronic hospital information system for information related to these diseases in the period after the diagnosis of CTS, and by verifying data obtained from the general practitioner.

To verify whether CTS may predict diabetes mellitus, hypothyroidism or CTD, positive predictive values (PPVs) of a CTS for the presence of these diseases were calculated, with a corresponding 95% confidence interval (CI). For the calculation of the PPVs of a CTS for diabetes mellitus, patients who have been diagnosed with this disease before and those in whom no blood glucose test was performed were excluded (fig 1). Similar separate analyses were performed for the calculation of the PPVs for hypothyroidism and CTD (fig 1).

RESULTS

Figure 1 shows the details of the 516 patients with CTS (Erasmus MC: 365, SFG Hospital: 151) who fulfilled the inclusion criteria for this study. The mean age for women was 50.8 years (range 25–95) and that for men 50.7 years (range 24–78). Of the 516 patients with CTS, 56 (11%) were previously diagnosed with diabetes mellitus, 30 (6%) had hypothyroidism and 44 (9%) had a CTD. Figure 1 shows the results of the additional blood tests in the CTS study population. Ten patients with CTS without previously diagnosed diabetes mellitus had raised glucose levels, of whom seven did not have de novo diabetes mellitus (normal glucose tolerance test, normal glucose levels at repeated tests, raised levels due to pregnancy). In seven patients with CTS with abnormal TSH levels, free thyroxine was normal. The causes of the raised ESR not related to CTD were several, including chronic infection, nephropathy and cancer.

The PPV of a CTS for diabetes mellitus in this study population was low, 0.5% (95% CI, 0.1 to 1.7). A total of 216 patients had to be tested to find one newly diagnosed patient with diabetes mellitus in a CTS population without previously known diabetes mellitus. The PPV of a CTS for hypothyroidism was 0.4% (95% CI, 0.1 to 1.5); 234 patients with CTS had to be tested to find one patient newly diagnosed with hypothyroidism.

Abbreviations: CTD, connective tissue disease; CTS, carpal tunnel syndrome; ESR, erythrocyte sedimentation rate; PPV, positive predictive value; SFG, Sint Franciscus Gasthuis; TSH, thyroid-stimulating hormone

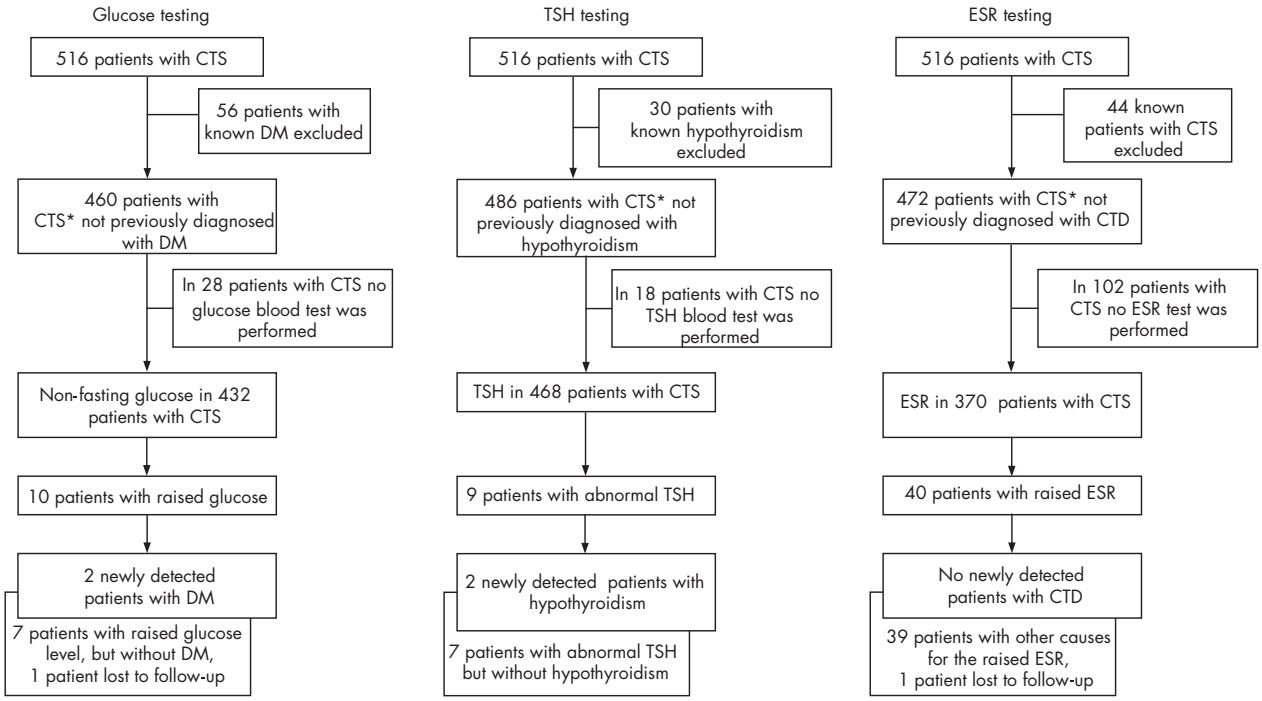

Figure 1 Results of additional blood testing. CTD, connective tissue disease; DM, diabetes mellitus; ESR, erythrocyte sedimentation rate; TSH, thyroid stimulating hormone. *The results are shown separately for each type of blood test for underlying unknown diseases in patients with carpal tunnel syndrome. †In each separate analysis, those who have been diagnosed before with the related disease have been excluded.

The PPV of a CTS for CTD in this study population was 0%. Among the 516 patients with CTS screened, only two patients with diabetes mellitus (one woman aged 34 years and one man aged 59 years) and two women (aged 28 and 47 years) with hypothyroidism were newly detected. None of these four de novo patients had a concurrent polyneuropathy.

DISCUSSION

In this study, we show that systematic screening for diabetes mellitus, hypothyroidism and CTD in patients with CTS who have not been diagnosed with these underlying diseases before leads to a limited number of newly detected patients. Consequently, CTS rarely seems to be the presenting symptom of previously undiagnosed diabetes mellitus, hypothyroidism and CTD. In only one other study, in which concurrent diseases in patients with CTS were investigated, was it verified whether the concurrent diagnosis of diabetes mellitus, hypothyroidism and CTD was made before or after the diagnosis of CTS.[9] However, this retrospective study was conducted in a selected population confined to patients with work-related CTS.

This study is a retrospective hospital-based study, which may yield some methodological limitations. Theoretically, selection of the study population might have occurred. The study comprised persons who had been referred to the neurologist because of complaints suggestive of CTS, and did not include those with CTS who go undetected in the population. In addition, only patients with CTS who underwent blood test screening for diabetes mellitus, hypothyroidism or CTD were included in this study. It is conceivable that among these hospital-based patients, a higher proportion have an underlying disease. Also, blood tests may have been conducted more often in those patients with CTS who were suspected of having an underlying, yet undetected, disease. Owing to a possible selection bias, and, as a consequence, a higher risk of having an underlying disease in this CTS study population, the PPVs in our study may have been overestimated rather than underestimated. Nevertheless, the PPVs and the number of de novo patients remained very low. Therefore, it is unlikely that a possible selection bias has influenced the results and our conclusions.

The strong points of our study are the large group of patients, selected from both a teaching hospital and a general hospital, and the very low number of patients lost to follow-up.

Based on our findings, the question arises as to whether it is useful to perform a systematic screening for underlying diseases in patients with typical CTS. One could argue that the costs of screening through three simple blood tests are low, and that early detection of diabetes mellitus, hypothyroidism or CTD could prevent some of the complications that may occur in the later stages of these diseases. In addition, CTS may be cured or CTS symptoms may diminish by treatment of these diseases, especially hypothyroidism. On the basis of our study sample, the estimated cost of detecting one de novo patient with hypothyroidism is €1468 (including the subsequent testing of false positive patients and excluding the costs of taking blood samples, personnel expenses and administration). For diabetes mellitus, these expenses are fourfold lower. As a result, cost-benefit analysis of additional blood tests, despite the low PPVs, might prove to be positive. However, the additional blood tests led to a very low number of newly detected patients with diabetes mellitus, hypothyroidism or CTD (<1%), especially in view of the prevalences of these diseases in the general population (4% for diabetes mellitus,[3] up to 9.5% for hypothyroidism[4] and up to 15% for CTD[5]) and in patients with CTS. In addition, a high percentage of false positive blood tests, as in our study, may cause an unacceptable burden to the patients. Notwithstanding these observations, additional blood tests may prove to be useful in patients with a clinical history suggestive of diabetes mellitus or thyroid dysfunction, and in those patients having an unusual clinical presentation—for example a male presenting with a recent double-sided CTS.

We conclude that, in general, CTS is rarely the presenting symptom of previously undiagnosed diabetes mellitus,

hypothyroidism and CTD. As a consequence, systematic screening for incident diabetes mellitus, hypothyroidism or CTD through additional blood tests is not recommended in typical patients with CTS without symptoms of any of these systemic disorders.

Authors' affiliations
Maarten C de Rijk, Maartje Suntjens, Pieter A van Doorn, Department of Neurology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands
Frederique H Vermeij, Department of Neurology, St Franciscus Gasthuis, Rotterdam, The Netherlands

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Correspondence to: Dr M C de Rijk, Department of Neurology, Catharina-ziekenhuis, PO Box 1350, 5602 ZA Eindhoven, The Netherlands; m.derijk@erasmusmc.nl

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